5. McKee JE, Wolf HW. *Water Quality Criteria* (Publication 3-A). 2nd ed. California: State Water Quality Control Board, 1963: 119.
6. Public Health Activities Committee, American Society of Civil Engineers. Coliform standards for recreational waters. *J San Eng Div, Proc Am Soc Civil Eng* 1963; **89:** 57.
7. Mechalas BJ, Hekiman KK, Schinazi LA, Dudley RH. *An Investigation into Recreational Water Quality: Water Quality Data Book,* vol. 4. Washington, DC: US Environmental Protection Agency, 1972: 20-23.
8. Committee on Water Quality Criteria. *Water Quality Criteria.* Washington, DC: National Academy of Sciences, Environmental Protection Agency, 1972: 30-32.
9. Moore B. A survey of beach pollution at a seaside resort. *J Hyg (Lond)* 1954; **52:** 71-86.
10. Flynn MJ, Thistlethwayte DKB. Sewage pollution and seabathing. *Int J Water Poll* 1965; **9:** 641-653.
11. Iwato T. Formal discussion. In: *Advances in Water Pollution Research,* vol. III. London: Pergamon, 1965: 15.
12. Livingstone DJ. An appraisal of sewage pollution along a section of the Natal coast. *J Hyg (Lond)* 1969; **67:** 209-223.
13. Lee JV, Bashford TJ, Donovan AL *et al.* The incidence of *Vibrio cholerae* in water, animals and birds in Kent, England. *J Appl Bacteriol* 1982; **52:** 281-291.
14. Livingstone DJ. An appraisal of sewage pollution along a section of the Natal coast after the introduction of submarine outfalls. *J Hyg (Lond)* 1976; **77:** 263-266.
15. Livingstone DJ. The effect of submarine wastewater discharge on the bacterial quality of surf waters. *Water Sci Technol* 1982; **14:** 1-11.

Shock lung — experimental studies on a haemorrhagic hypovolaemic rabbit model

F. M. ENGELBRECHT, W. L. MOUTON, L. J. VAN SCHALKWYK

Summary

An experimental model of haemorrhagic hypotension was standardized using rabbits to investigate the shock lung syndrome over a period of 120 minutes. Acute hypovolaemia was induced by withdrawal of blood under anaesthesia to a mean arterial pressure of 30 ± 5 mmHg within 10 minutes. The mean leucocyte counts and the release of lysosomal enzymes (acid phosphatase and ß-glucuronidase) in the blood and in lung tissue, as well as the metabolic capacities of lung tissue in terms of protein and lipid biosynthesis, were investigated at set intervals after 30, 60, 90 and 120 minutes.

The results indicate a progressive decline in leucocyte numbers over 120 minutes to about 40% of the original. An immediate granulocytopenia was observed with a relative lymphocytosis within 30 minutes. The ß-glucuronidase and acid phosphatase contents of the plasma increased with time; ß-glucuronidase activity increased progressively as leucocytes disappeared from the circulation. Concomitantly, the capacity of the lung tissue to synthesize protein and lipids was retarded with time, becoming significantly lower than baseline values after 60 minutes of hypovolaemia. The decline in leucocyte numbers in the circulation correlated well with the increase in ß-glucuronidase activity and the retarded metabolic capacity of the lung tissue.

S Afr Med J 1983; **64:** 400-404.

Department of Medical Physiology and Biochemistry, University of Stellenbosch, Parowvallei, CP
F. M. ENGELBRECHT, D.SC.
W. L. MOUTON, M.B. CH.B.
L. J. VAN SCHALKWYK, B.SC.

Date received: 6 September 1982.

The shock lung syndrome was first recognized during World War I and is occurring with increasing frequency in patients who have been resuscitated after severe haemorrhage and in those suffering from endotoxic shock. Shock, whether due to sepsis, haemorrhage or trauma, is an acute syndrome of cardiovascular failure in which the basic pathological derangement is inadequate tissue perfusion. The available evidence indicates that shock is characterized not by reduced blood flow but by maldistribution of blood flow.[1]

The lung's first reaction to shock is constriction of the pulmonary arterioles, followed by damage to the vascular endothelium, increased permeability of the microcirculation, and leakage of protein-containing fluid into the interstitial spaces and alveoli. Concurrent degeneration of alveolar cells contributes to intra-alveolar oedema.[2]

The mechanisms involved in alveolar and endothelial capillary damage may be as follows: formation of microthrombi at the sites of injury and activation of the complement cascade resulting in leucocyte aggregation and accumulation in lung capillaries with release of inflammatory mediators, lung ischaemia and oxygen toxicity.[3] According to Gaffin[4] the irreversible phase of haemorrhagic shock is due to invasion of the blood by endotoxins from the intestines. The most important effect of the endotoxins is the massive increase in the level of circulating vasoactive agents, including prostaglandins, catecholamines, histamine, kinins and serotonin, mediated in part by granulocytes.[4] Release of a low-molecular-weight myocardial depressant factor into the systemic circulation from the splanchnic area as a result of hypoxia may also be involved. Recently it was demonstrated that the rate of phosphatidylcholine synthesis in the lungs of animals suffering from septicaemia decreased.[5]

Lysosomal enzymes released from sequestered and fragmented leucocytes in the lungs during haemorrhage or endotoxaemia could damage the endothelial membranes and cross into the interstitium. During fatal haemorrhage and after endotoxin administration in sheep, ß-glucuronidase increased by 100% in plasma and by 400 - 600% in lung lymph.[6] Apart from lysosomal enzymes, leucocytes may release superoxide radicals which damage the microvascular membrane. Products of the lipoxygenase pathway, i.e. hydroperoxy fatty acids, hydroxy fatty acids

and leukotrienes, have potent leucocyte chemotactic properties and stimulate leucocyte degranulation.[7]

Increased endothelial permeability in shock lung syndrome has also been attributed to the action of platelets, and platelet sequestration has been demonstrated in the lung after exposure to high altitudes, trauma and shock. Recently[8] it was shown that increased platelet sequestration during haemorrhagic shock is related to decreased blood flow rather than to adherence to the endothelium. The view that platelets are necessary in the pathogenesis of pressure oedema is therefore no longer valid.[8]

The pulmonary capillary endothelial cell is involved in several metabolic functions. During acute hypoxia the conversion of angiotensin II is retarded whereas the concentration of bradykinin is elevated, resulting in increased levels in the blood. These changes during hypoxia are associated with a sustained increase in pulmonary vascular permeability to proteins and water. The vascular endothelium is also responsible for the pulmonary removal of serotonin and noradrenaline from the blood by transcellular uptake and metabolism. It has been suggested that the uptake of these amines might provide a metabolic index of endothelial cell function.[9] Recently[10] it was shown that isolated lung tissue is extremely sensitive to hypoxic damage and that oxygen uptake and the biosynthesis rate of lipids and proteins were markedly depressed by hypoxia.

It is generally accepted that endothelial capillary damage and possibly damage to other cell types are early manifestations of shock lung. If so, it should be possible to assess the degree of cellular damage by measuring the biosynthetic capacity of lung tissue after different periods of shock.

In the present investigation, the following parameters were studied during experimental haemorrhagic shock: (*i*) biosynthesis rates of lung tissue lipids and proteins after various periods of hypovolaemia; (*ii*) acid phosphatase and ß-glucuronidase activity in the serum and lung tissue; and (*iii*) changes in haematocrit and in leucocyte counts.

Material and methods

New Zealand White rabbits (1,6 ± 0,2 kg) were used to study several parameters of shock lung resulting from acute haemorrhagic hypovolaemic shock. The animals were weighed and anaesthetized by injecting 2,5% thiopentone sodium (30 mg/kg body weight) via an intravenous catheter needle (20G, 38 mm) clamped in position in the ear vein.

The anaesthetized animal was transferred in a supine position to an operating table kept at a constant temperature (38°C). An incision was made in the middle neck after injecting 1% lignocaine subcutaneously into the neck area. Tracheotomy was performed and a cannula (diameter 3,5 mm, length 50 mm) was inserted into the trachea to ensure free breathing.

The right carotid artery was dissected and separated from the vagus and sympathetic nerves. A polyethylene catheter, fitted with a Luer-lock connection on one end and filled with heparinized saline (15 U/ml) was inserted into the carotid artery and secured after clamping the artery. A three-way tap was fitted into the Luer-lock connection. One opening was attached to a polyethylene tube filled with heparinized saline from a pressure bottle leading from a mercury manometer (Clay Adams), while a 20 ml syringe was fitted to the other opening for the withdrawal of blood.

The surgical procedure was completed within 10 minutes. The clamped carotid artery was released and the blood pressure was monitored for the duration of the experiment. After a stabilization period of 10 minutes the normal blood pressure was noted. Immediately afterwards blood was withdrawn by means of the syringe to an arterial pressure of 30 mmHg over a period of 10 minutes (zero time). Since compensation for blood loss occurred with time, it was necessary to withdraw additional small volumes of blood to maintain an average arterial pressure of 30 ± 5 mmHg over periods of 30, 60, 90 and 120 minutes.

On termination of the predetermined hypotensive period the rabbit was killed by exsanguination and the lungs were immediately perfused *in situ* with 50 ml cold phosphate-buffered saline via the pulmonary artery while the lungs were ventilated with air by means of a 50 ml syringe attached to the tracheal cannula. The lungs and heart were dissected *en bloc* and transferred to ice-cold saline until further processing.

Blood analysis

Two blood samples were taken from each animal at zero time and on termination of the experiment at 30, 60, 90 or 120 minutes. One sample was heparinized and used for determination of total leucocyte counts, differental counts and haematocrit values. The other sample was allowed to clot and serum was prepared for the determination of the ß-glucuronidase and acid phosphatase activities according to the methods of Bergmeyer and Gawehn.[11]

Lung analysis

A control rabbit of approximately the same age and weight as the experimental rabbit was bled to death under anaesthesia and the lungs were perfused, removed and stored in cold saline. Both the control and experimental lung lobes were sliced with a McIlwain tissue chopper into 0,7 mm slices after the trachea and bronchi had been dissected out.

The following samples from each lung were weighed carefully:

1. Three 300 mg samples for the determination of ß-glucuronidase and acid phosphatase activity in lung tissue. Each portion was suspended in 5 ml de-ionized water containing 0,1% Triton X 100, and sonicated for four periods of 15 seconds (Heat Systems Ultrasonic Inc.). The sonicates were centrifuged at 10 000 *g* for 10 minutes. The supernatants were used for enzyme determinations in triplicate according to the methods of Bergmeyer and Gawehn,[11] and also for protein determinations.[12]
2. Three 100 mg slices were used for determination of the rate of incorporation of ^{14}C-leucine into lung proteins as described previously.[10]
3. Three 300 mg slices were used for determination of the rate of incorporation of ^{14}C-palmitate into the lipids of lung slices as described previously.[10]
4. Three 100 mg slices from each lung were used for estimation of the DNA content according to the method of Burton.[13]

The experiment was repeated 10 times at each time interval and individual estimations were done in triplicate. Standard methods were used to compute the mean and the standard error of the mean. Pairwise comparisons were made using a two-sided Student's *t* test.

Results

Maintenance of an arterial blood pressure of 30 ± 5 mmHg, irrespective of the volume of blood drawn, was the principle used to induce acute haemorrhagic hypotension. Before zero time all rabbits had pH, blood pressure, pulse rate, haemoglobin, partial arterial carbon dioxide (P_{CO_2}) and total CO_2 values well within the normal range specified by Spector.[14] These parameters and others were previously studied in a similar shock model and are therefore not included in the present investigation.[15]

The changes in haematocrit and total and differential leucocyte counts as well as the values corrected for haemodilution are summarized in Table I. The total leucocyte count dropped from a mean control value of 7 845 ± 435/µl to 1 818 ± 335/µl at 120 minutes. At the same time the haematocrit decreased from 0,39 to 0,23, which indicates a marked haemodilution. From the

corrected leucocyte numbers, this represents a sharp drop from 100% to 46,1% leucocytes during the first 30 minutes followed by a gradual further decrease to 40% at 120 minutes. Haemodilution therefore could not account for the loss of leucocytes from the circulation. The most striking observation from Table I is the drastic decrease in the percentage and number of granulocytes in the circulation at 30 minutes. At this stage a granulocytopenia was found and the leucocyte count therefore showed a relative lymphocytosis. From 30 minutes onwards the percentage of granulocytes rose, reaching a normal percentage distribution at 120 minutes. This could indicate a gradual increase in the granulocyte count in the circulation. Although a relative lymphocytosis was found 30 minutes after withdrawal of blood, the actual numbers of lymphocytes in the circulation in fact decreased between zero time and 120 minutes. At this stage the percentage distribution of granulocytes and lymphocytes had almost returned to normal, although their total numbers in the circulation were reduced to 40% of control values.

Table II summarizes the ß-glucuronidase and acid phosphatase activities in lung tissue and serum of animals subjected to hypovolaemia (mean arterial blood pressure 30 ± 5 mmHg) for 30, 60, 90 and 120 minutes. Each animal served as its own control. This experimental design was arranged to compensate for the large individual variation between animals.

In lung tissue, acid phosphatase activity (μmol/g protein/min at 25°C) increased significantly at 30 minutes; and ß-glucuronidase activity also increased but to an insignificant extent. The values obtained for both enzymes in lung tissue at 60, 90 and 120 minutes were not significantly different from control values.

Acid phosphatase values in serum (μmol/l/min at 25°C) were significantly lowered at 30 minutes and showed the same tendency at 60, 90 and 120 minutes. When corrected for haemodilution, these values increased significantly at all time intervals except at 90 minutes.

The ß-glucuronidase activity (μmol/l/min at 37°C) in serum was significantly higher than baseline values at all time intervals. With correction for haemodilution, the difference from baseline values became highly significant, except at 120 minutes.

The mean rates of protein and lipid biosynthesis in control and hypovolaemic rabbit lung tissue after 30, 60, 90 and 120 minutes are summarized in Table III. The rates of protein and lipid synthesis showed no significant differences between control and experimental values after 30 and 60 minutes of hypovolaemia. After 90 and 120 minutes, however, protein and lipid biosynthesis were significantly depressed.

Discussion

An experimental model of haemorrhagic hypotension was standardized using rabbits to investigate some metabolic parameters in lung tissue which may be quantitative indicators of the severity of lung damage after hypovolaemic shock. Changes in leucocyte counts and lysosomal enzyme concentrations in lung tissue and in the blood of the same animals were also measured and correlated with metabolic parameters after set intervals of 30, 60, 90 and 120 minutes of hypovolaemia.

This time schedule was chosen to follow the changes in enzyme concentrations, leucocyte counts and lung damage systematically in an attempt to define the demarcation line between reversible and irreversible shock.

Within the arterial pressure range chosen, blood loss was equivalent to 35,9 ± 0,70% of the total blood volume. Under this condition death takes place soon after 120 minutes of hypovolaemia. Some animals even died before the predetermined time, usually from a sudden fall in blood pressure which might indicate heart failure.

Our results indicate a drastic fall in the leucocyte count (even after correction for haemodilution) within 30 minutes of hypovo-

TABLE I: HAEMATOCRIT AND TOTAL AND DIFFERENTIAL LEUCOCYTE COUNTS AT ZERO TIME AND AFTER 30, 60, 90 AND 120 MINUTES OF HYPOVOLAEMIA (MEAN ARTERIAL PRESSURE 30 ± 5 mmHg)*

Duration of hypovolaemia (min)	Haematocrit	Leucocyte count (/μl)	Leucocyte count (/μl)†	% distribution		Differential leucocyte count†		% leucocytes remaining†
				Granulocytes	Lymphocytes	Granulocytes (/μl)	Lymphocytes (/μl)	
0	0,397 ± 0,006	7 845,0 ± 435,4	7 845,0 ± 435,4	50,3 ± 1,69	49,7 ± 1,69	3 946,0	3 898,9	100,0
30	0,27 ± 0,0052	2 460,0 ± 119,7	2 617,2 ± 176,0	18,1 ± 2,14	81,9 ± 2,14	654,7	2 962,5	46,11
60	0,255 ± 0,0034	2 190,0 ± 182,4	3 409,6 ± 283,9	31,8 ± 2,87	68,2 ± 2,87	1 084,3	2 325,3	43,46
90	0,241 ± 0,0079	1 909,0 ± 143,2	3 144,7 ± 235,9	47,1 ± 3,36	52,9 ± 3,36	1 481,2	1 663,5	40,09
120	0,230 ± 0,0032	1 818,0 ± 334,7	3 138,1 ± 577,7	49,0 ± 5,75	51,0 ± 5,75	1 562,2	1 600,4	40,0

*Mean ± SE of 10 animals at each time interval.
†Corrected for haemodilution.

TABLE II. BETA-GLUCURONIDASE AND ACID PHOSPHATASE ACTIVITIES IN LUNG TISSUE (μmol/g protein/min) AND IN THE SERUM OF RABBITS (μmol/l/min) AT ZERO TIME AND AFTER 30, 60, 90 AND 120 MINUTES OF HYPOVOLAEMIA (MEAN ARTERIAL PRESSURE 30 ± 5 mmHg)

	30 min		60 min		90 min		120 min	
	Control	Shock	Control	Shock	Control	Shock	Control	Shock
ß-glucuronidase								
Lung tissue values	0,16 ± 0,026	0,23 ± 0,015	0,16 ± 0,034	0,18 ± 0,027	0,15 ± 0,018	0,19 ± 0,097	0,17 ± 0,013	0,16 ± 0,02
Serum values†	95,0 ± 7,78	168,4 ± 16,52§	99,2 ± 31,72	216,4 ± 32,68*	99,0 ± 9,84	319,0 ± 28,07*	108,0 ± 5,21	546,8 ± 115,82*
Corrected serum values‡	95,0 ± 7,78	247,6 ± 24,28§	99,2 ± 31,72	336,9 ± 50,89§	99,0 ± 9,84	525,5 ± 46,23§	108,0 ± 5,21	943,8 ± 199,9*
Acid phosphatase								
Lung tissue values	25,4 ± 1,86	31,0 ± 1,52*	25,2 ± 2,06	24,6 ± 1,33	27,2 ± 2,48	31,4 ± 3,41	28,2 ± 1,02	28,6 ± 2,34
Serum values†	89,8 ± 5,95	73,0 ± 4,25§	89,8 ± 6,82	77,2 ± 7,95	93,4 ± 9,11	68,6 ± 7,38	97,0 ± 3,21	77,8 ± 5,70
Corrected serum values‡	89,8 ± 5,95	107,3 ± 6,25§	89,8 ± 6,82	120,2 ± 12,37*	93,4 ± 9,11	113,0 ± 12,16	97,0 ± 3,21	134,3 ± 9,85*

*$P < 0,05$.
§$P < 0,01$.
†Mean ± SE of at least 10 animals, which served as their own controls at zero time. All estimations were done in triplicate.
‡Serum values corrected for haemodilution using mean haematocrit values estimated at each time interval of hypovolaemia.

TABLE III. RATES OF PROTEIN AND LIPID BIOSYNTHESIS OF RABBIT LUNG TISSUE (DPM/mg DNA/h) AFTER 30, 60, 90 AND 120 MINUTES OF HYPOVOLAEMIC SHOCK (MEAN ARTERIAL PRESSURE 30 ± 5 mmHg)

	30 min		60 min		80 min		120 min	
	Control	Shock	Control	Shock	Control	Shock	Control	Shock
Protein synthesis	20 933,3 ± 1 493,3	19 600,0 ± 2 090,0*	20 200,0 ± 933,3	16 333,3 ± 2 060,0*	18 400,0 ± 933,3	14 733,3 ± 356,7§	19 466,7 ± 680,0	12 600,0 ± 826,7$
Lipid synthesis	13 266,7 ± 413,3	13 133,3 ± 806,7*	13 000,0 ± 366,7	10 666,7 ± 1 303,3*	12 466,7 ± 480,0	9 000,0 ± 6,13,3$	13 200,0 ± 556,7	9 000,0 ± 236,7‡

*$P > 0,05$.
§$P < 0,005$.
$P < 0,01$.
‡$P < 0,001$.
†Mean ± SE. At least 10 animals were used in control and shock experiments. All estimations were done in triplicate.
DPM = disintegrations per minute.

laemia to 46,1% of the control value. The sharp decrease in the percentage of granulocytes was especially noticeable. These cells were possibly sequestered and fragmented in the microcirculation with the release of microsomal enzymes.[7] However, after little more than 30 minutes the granulocytes reappeared in the circulation, either from sequestered cells in the microcirculation or from the bone marrow. An increase in band cells was found, which might imply that the bone marrow was a possible source.

Owing to the differential sequestration of granulocytes during the early stage of hypovolaemia a relative lymphocytosis was observed. However, the number of lymphocytes also gradually decreased with time to about 40% of the baseline count within 120 minutes. The fate of these lymphocytes is uncertain, but it has been suggested that some are aggregated in the microcirculation of the lung with the release of inflammatory mediators.[3]

If the vanished leucocytes were trapped in the microcirculation one would expect to find a significant increase in DNA content and in the levels of both lysosomal enzymes measured in lung tissue. However, our results showed only a significant increase in acid phosphatase activity at 30 minutes. This might be due to the fact that all the lungs were perfused to deplete them of blood for further metabolic experiments. Cells trapped in the microcirculation could therefore have been washed out.

Extrapolation from our control values showed that the ß-glucuronidase content in lung tissue is about 8 times lower than in the plasma of the same animal, whereas the acid phosphatase content of lung tissue is almost 20 times higher than that of plasma. However, plasma ß-glucuronidase content significantly and progressively increased during hypovolaemia. This increase correlated well with the disappearance of leucocytes and the duration of hypovolaemia. The acid phosphatase activity of lung tissue increased significantly after 30 minutes of hypovolaemia but thereafter remained within normal baseline limits. True plasma values on the other hand were significantly lower over the whole of the hypovolaemic period. When these values were corrected for haemodilution the changes at most time intervals reached significance ($P < 0,05$). However, the increase in plasma acid phosphatase values did not correlate well with the disappearance of leucocytes from the circulation. It would therefore appear that ß-glucuronidase and acid phosphatase are differentially released by leucocytes or by different cell types altogether.

The rates of both protein and lipid biosynthesis in lung tissue were gradually lowered up to 60 minutes, the changes reaching significance at 90 minutes, with highly significant differences at 120 minutes. Apart from lactic acid accumulation[15] and a decrease in total body oxygen consumption,[1] this is the first time metabolic injury to lung tissue has been demonstrated as a result of haemorrhagic hypovolaemia. The cell injury could be caused by the activation of lysosomal enzymes, i.e. ß-glucuronidase, proteinases and phospholipases. The latter enzymes would enhance protein and lipid degradation respectively, thus retarding the measured protein and lipid biosynthesis rates. Whatever the case may be, the activation of lysosomal enzymes is probably due to the sustained hypoxia. Recently it has been shown that lung tissue is extremely sensitive to hypoxia at body temperatures leading to metabolic injury.[10] Our results agree with the findings of Hohn *et al.*,[16] who also demonstrated a drastic decrease in polymorphonuclear leucocytes in the circulation upon infusion of complement-activated plasma. The granulocytes were aggregated, forming pulmonary vascular plugs, which resulted in shunting of blood and lung tissue hypoxia. Degeneration of these aggregates could lead to the release of lysosomal enzymes which caused the observed metabolic injury.

From our results it would appear that the following are most significant as indicators of irreversible shock in the rabbit: (*i*) severe hypovolaemia for 1 hour or longer; (*ii*) elevation of ß-glucuronidase and acid phosphatase activities in the blood above 240% and 34% respectively; (*iii*) reduction of leucocyte numbers in the circulation below 44% of control values; and (*iv*) inhibition of protein and lipid biosynthesis rates of lung tissue by 20% or more.

We wish to express our gratitude to the South African Medical Research Council and the Nuclear Development Corporation of South Africa for financial assistance and to Mrs M. L. Windt, Miss E. Badenhorst and Mr M. Blom for technical assistance.

REFERENCES

1. Schoemaker WC. *Shock in Low- and High-Flow States.* Amsterdam, Excerpta Medica: 1972, 119-130.
2. Moss GS, Newson B, Das Gupta TK. The normal electron histochemistry and the effect of hemorrhagic shock on the pulmonary surfactant system. *Surg Gynecol Obstet* 1975; **140:** 53-58.
3. Lund T, McDonald JA, Avioli LV. Adult respiratory distress syndrome. *Arch Intern Med* 1981; **141:** 1749-1753.
4. Gaffin SL. Control of septic shock — present day concept. *S Afr J Hosp Med* 1982; **8:** 4-11.
5. Von Wichert P, Temmesfeld M, Meyer W. Influence of septic shock upon phosphatidyl-choline remodelling mechanism in rat lung. *Biochim Biophys Acta* 1981; **664:** 487-497.
6. Demling RH, Proctor R, Duy N, Starling JR. Lung lysosomal enzyme release during hemorrhagic shock and endotoxemia. *J Surg Res* 1980; **28:** 269-279.
7. Smith M, Gunther R, Zaiss C, Flynn J, Dunling R. Pulmonary microvascular injury from lipoxygenase infusion: comparison with endotoxemia. *Circ Shock* 1981; **8:** 647-656.
8. Martin BA, Dahlby R, Nichols I, Hogg JC. Platelet sequestration in lung with hemorrhagic shock and reinfusion in dogs. *J Appl Physiol* 1981; **50:** 1306-1312.
9. Block ER, Stalcup AS. Today's practice of cardiopulmonary medicine: metabolic functions of the lung, of what clinical relevance? *Chest* 1982; **81:** 215-223.
10. Engelbrecht FM, Edward IJ, De Beer DP. Metabolic changes in the lungs after ischaemia. *S Afr Med J* 1980; **58:** 409-414.
11. Bergmeyer HU, Gawehn K. *Methods in Enzymatic Analysis,* vol. 2. 2nd ed. New York: Academic Press, 1974: 858-859, 934-936.
12. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurements with the folin reagent. *J Biol Chem* 1951; **193:** 265-275.
13. Burton K. A study of the conditions and mechanisms of the diphenylamine reaction for the colorimetric estimation of deoxyribonucleic acid. *Biochem J* 1956; **62:** 315-323.
14. Spector WS. Acid base balance: vertebrates. In: Spector WS, ed. *Handbook of Biological Data.* London: WB Saunders, 1959: 271.
15. Costa N. Haemodynamic and biochemical changes occurring during haemorrhagic hypotensive shock (M.Sc. thesis). University of Stellenbosch, 1979.
16. Hohn DC, Meyers AJ, Gherini ST, Beckman A, Markison RE, Churg AM. Production of acute pulmonary injury by leucocytes and activated complement. *Surgery* 1980; **88:** 48-58.